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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,074	02/15/2002	Matthew C. Coffey	032775-091	8498

26181 7590 08/23/2005

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EXAMINER
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LI, BAO Q

ART UNIT	PAPER NUMBER
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1648

DATE MAILED: 08/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/076,074	<b>Applicant(s)</b> COFFEY ET AL.	
	<b>Examiner</b> Bao Qun Li	<b>Art Unit</b> 1648	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

**A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.**

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 14 January 2005.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) 31-34 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-30 is/are rejected.
- 7) ☒ Claim(s) 26 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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## **DETAILED ACTION**

### **RCE**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 07/13/2005 has been entered. The RCE follows:

### ***Response to Amendment***

The amendment filed 01/14/2005 have been acknowledged. Claims 1 and 26 have been amended. Claims 1-34 are pending. Claims 1-30 are considered. Claims 31-34 are withdrawn from the consideration.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

### ***New Matter Objection***

The amendment filed on 01/14/2005 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material, which is not supported by the original disclosure is as follows: (1). Claim 26, step (a): "identifying a subject that harbors ras-activated neoplastic cells susceptible to a chemotherapeutic agent" Applicant is required to cancel the new matter in the reply to this Office Action.

### ***New Matter Rejection***

Claims 26-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

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In the instant case, the amendment of claim 26, step (a): “ identifying a subject that harbors ras-activated neoplastic cells susceptible to a chemotherapeutic agent” has not been disclosed in the application as it was originally filed. Applicants asserted that the support for this amendment can be found in the claim 26 as it was originally filed. Applicants argument has been fully considered, however, it is not persuasive because original claim 26 does not contain such active steps for identification of a subject 1) having a ras-active neoplasm, and 2) being susceptible to a chemotherapeutic agent also. The original claim 26 is only directed to administering reovirus and effective amount of chemotherapeutic agent to a subject. Therefore, claim 26 is rejected as new matter under 35 U.S.C. 112, first paragraph.

Because claims 27-30 are dependent claims of claim 26, they contains the new step is not supported by the disclosure of the specification as it was originally filed. They are rejected too accordingly.

### ***Double Patenting***

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).
2. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).
3. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

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4. Claims 1-6, 8-11, 12-13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 are still rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 28 of U.S. Patent No. 6,565,831B1) in view of disclosure of Smith (Exp. Opin. Invest. Drugs, 2000, Vol. 9, No. 2, pages 311-327).

5. An obviousness-type double-patenting rejection is appropriate where the conflict claims are not identical but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim(s) is either anticipated by or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 14U F.3d 1428, 46 USPQZd 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQZd 2010 (Fed. either anticipated by, 1993); *In re Longi*, F.2d 887, 225 US/Q 645 (Fed. Cir. 1985).

6. In the instant case, Applicants traverse the rejection and submit that none of the patent "831" claims discloses or suggests an amount for the chemotherapeutic agent being at least 20% less than the amount required in the absence of reovirus. They do not provide expectation of a reasonable expectation of a success by using less therapeutic agent when the reovirus is used.

7. Applicants' argument has been respectfully considered; however, it is not found persuasive because reducing an effective amount of the therapeutic agent rather than changing the therapeutic agent can be practically tested without undue experimentation by any person skill in the art. The modification of working condition is generally recognized as being within the level of the ordinary skill in the art, *In re Rose*, 105 USPQ 237 (CCPA 1995), and discovery of the workable ranges involves only routine skill in the art, *In re Aller*, 105, USPQ 233. It is well known in the art that oncolytic reovirus treatment of cancer is particularly susceptible and effective for the ras-mutated cancer, and combined oncolytic reovirus and a chemotherapeutic agent treatment is more superior to any of the agent used alone. For reovirus, such synergistic therapeutic effect can produce a rate of 80% complete tumor remission (See Smith et al. on pages 319, 1<sup>st</sup> paragraph of section 7 and 1<sup>st</sup> paragraph of section 9 on page 321). Therefore, it would have been obvious for a person with ordinary skill in the art to use less dosage of therapeutic agent in combination of the oncolytic reovirus for getting much better anti-tumor effect absence unexpected results.

8. Hence claimed invention would have been obvious over, the reference claim(s) in view of the disclosure by Smith et al.

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9. Claims 1-6, 8-11, 12-13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25 are still rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3-8, 13-20, 24-33 and 34 of U.S. Patent No. 6,136,307A) in view of the disclosure of Smith (Exp. Opin. Invest. Drugs, 2000, Vol. 9, No. 2, pages 311-327).

10. An obviousness-type double-patenting rejection is appropriate where the conflict claims are not identical but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim(s) is either anticipated by or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 14U F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. either anticipated by, 1993); *In re Longi*, F.2d 887, 225 US/Q 645 (Fed. Cir. 1985).

11. In the instant case, Applicants traverse the previous ODP rejection and submit that claims in patent "307" do not disclose administering an effective amount of a chemotherapeutic agent that is at least 20% less than the amount required in the absence of reovirus. Claims of the "307" patent also provide no motivation or suggestion to modify or a reasonable expectation of success. Therefore, the presently claimed invention is not obvious in view of the claims of the "307" patent.

12. Applicants' argument has been respectfully considered; however, it is not found persuasive because reducing an effective amount of a therapeutic agent rather than changing to another therapeutic agent can be practically approached without undue experimentation by any person skill in the art. The modification of working condition is generally recognized as being within the level of the ordinary skill in the art, *In re Rose*, 105 USPQ 237 (CCPA 1995), and discovery of the workable ranges involves only routine skill in the art, *In re Aller*, 105, USPQ 233. It is well known in the art that oncolytic reovirus treatment of cancer is particularly susceptible and effective for the ras-mutated cancer, and combined oncolytic reovirus and a chemotherapeutic agent treatment is more superior to any of the agent used alone. For reovirus, such synergistic therapeutic effect can produce a rate of 80% complete tumor remission (See Smith et al. on pages 319, 1<sup>st</sup> paragraph of section 7 and 1<sup>st</sup> paragraph of section 9 on page 321). Therefore, it would have been obvious for a person with ordinary skill in the art to use less dosage of therapeutic agent in combination of the oncolytic reovirus for getting much better anti-tumor effect absent unexpected results.

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13. Hence claimed invention would have been obvious over, the reference claim(s) in view of the disclosure by Smith et al.

***Claim Rejections - 35 USC § 103***

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

15. Claims 1-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (US Patent No. 6,136,307A) in view of Smith (Exp. Opin. Invest. Drugs, 2000, Vol. 9, No. 2, pages 311-327).

16. In attempting to overcome the 102 rejection, applicants have amended the claims 1 and 26, and submitted that “307 patent” does not teach a method of treating a ras-mediated proliferation disorder using at least 20% less amount of a therapeutic agent than that absence of reovirus treatment in claim 1 and comprising identifying a subject that harbors ras-activated neoplastic cells susceptible to a chemotherapeutic agent in claim 26.

17. Applicants’ argument has been respectfully considered; however, it is not found persuasive because regarding to claim 1, the modification of working condition is generally recognized as being within the level of the ordinary skill in the art, In re Rose, 105 USPQ 237 (CCPA 1995), and discovery of the workable ranges involves only routine skill in the art, In re Aller, 105, USPQ 233. Because it is known in the art that oncolytic reovirus treatment of cancer is particularly susceptible and effective for the ras-mutated cancer, and combined oncolytic reovirus and a chemotherapeutic agent treatment is more superior to any of the agent used alone. For reovirus, such synergistic therapeutic effect can produce a rate of 80% complete tumor remission (See Smith et al. on pages 319, 1<sup>st</sup> paragraph of section 7 and 1<sup>st</sup> paragraph of section 9 on page 321).

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18. Therefore, it would have been obvious for a person with ordinary skill in the art to be motivated using less dosage of therapeutic agent in combination of the oncolytic reovirus to treat ras-mediated neoplasm with much better anti-tumor effect since reovirus is particularly suitable for oncolyzing the ras-mediated neoplastic cell and combination of reovirus with a chemotherapeutic agent produces a synergistic effect. The claimed invention is *prima facie* obvious absence unexpected results.

19. Claims 1-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (WO 00/50051A2) in view of Smith et al. (Exp. Opin. Invest. Drugs, 2000, Vol. 9, No. 2, pages 311-327).

20. In attempting to overcome the 102 rejection, applicants have amended the claims 1 and 26, and submitted that “307 patent” does not teach a method of treating a ras-mediated proliferation disorder using at least 20% less amount of a therapeutic agent than that absence of reovirus treatment in claim 1 and comprising identifying a subject that harbors ras-activated neoplastic cells susceptible to a chemotherapeutic agent in claim 26.

21. Applicants’ argument has been respectfully considered; however, it is not found persuasive because regarding to claim 1, the modification of working condition is generally recognized as being within the level of the ordinary skill in the art, *In re Rose*, 105 USPQ 237 (CCPA 1995) and discovery of the workable ranges involves only routine skill in the art, *In re Aller*, 105, USPQ 233. Because it is known in the art that oncolytic reovirus treatment of cancer is particularly susceptible and effective for the ras-mutated cancer, and combined oncolytic reovirus and a chemotherapeutic agent treatment is more superior to any of the agent used alone. For reovirus, such synergistic therapeutic effect can produce a rate of 80% complete tumor remission (See Smith et al. on pages 319, 1<sup>st</sup> paragraph of section 7 and 1<sup>st</sup> paragraph of section 9 on page 321).

22. Therefore, it would have been obvious for a person with ordinary skill in the art to be motivated using less dosage of therapeutic agent in combination of the oncolytic reovirus to treat ras-mediated neoplasm with much better anti-tumor effect. The claimed invention is *prima facie* obvious absence unexpected results.



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23. Claims 1-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (Exp. Opin. Invest. Drugs, 2000, Vol. 9, No. 2, pages 311-327).

24. The claimed invention is directed to a method of sensitizing Ras-activating neoplastic cells in a mammal comprising administration of an effective amount of reovirus to increase the sensitivity of the therapeutic agent and the chemotherapeutic agent with at least 20% less amount than what it is required in the absence of the reovirus.

25. Smith et al. teach that oncolytic reovirus treatment of cancer is particularly susceptible and effective for the ras-mutated cancer, and combined oncolytic reovirus and a chemotherapeutic agent treatment is more superior to any of the agent used alone. For reovirus, such synergistic therapeutic effect can produce a rate of 80% complete tumor remission (See pages 319, 1<sup>st</sup> paragraph of section 7 and 1<sup>st</sup> paragraph of section 9 on page 321).

26. Regarding to the precise number of less than 20% amount, applicants are reminded that the modification of working condition is generally recognized as being within the level of the ordinary skill in the art, In re Rose, 105 USPQ 237 (CCPA 1995), and discovery of the workable ranges involves only routine skill in the art, In re Aller, 105, USPQ 233.

27. Therefore, it would have been obvious for a person with ordinary skill in the art to be motivated using less dosage of therapeutic agent in combination of the oncolytic reovirus to treat ras-mediated neoplasm with much better anti-tumor effect since reovirus is particularly suitable for oncolyzing the ras-mediated neoplastic cell and combination of reovirus with a chemotherapeutic agent produces a synergistic effect. The claimed invention is prima facie obvious absence unexpected results.

28. Claims 1-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mercer University (Mercer University Home page 1996, pp. 1-2) in view of Smith et al. (Exp. Opin. Invest. Drugs, 2000, Vol. 9, No. 2, pages 311-327).

29. Mercer University published on its home page that disclose that Dr. Steele give mice a combination of reovirus type 3 and a chemotherapeutic compound BCUN, resulting in 100% implanted tumor reduction (see entire document). Regarding to the limitations of the recitation of “sensitizing” or “preventing” a neoplastic cell to a chemotherapeutic agent, Office considered these recitation as preamble languages, which do not change the manipulating steps of the

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method comprising administration of reovirus and a chemotherapeutic agent into a population of neoplastic cells that result in a reduction of the neoplastic cells growth in vitro or in vivo. Mercer University does not teach that the reovirus is suitable for using with reovirus, and combination of reovirus and a chemotherapeutic agent can reduce the dosage of the chemotherapeutic agent.

30. Smith et al. teach that oncolytic reovirus treatment of cancer is particularly susceptible and effective for the ras-mutated cancer, and combined oncolytic reovirus and a chemotherapeutic agent treatment is more superior to any of the agent used alone. For reovirus, such synergistic therapeutic effect can produce a rate of 80% complete tumor remission (See pages 319, 1<sup>st</sup> paragraph of section 7 and 1<sup>st</sup> paragraph of section 9 on page 321).

31. Regarding to the precise number of less than 20% amount, applicants are reminded that the modification of working condition is generally recognized as being within the level of the ordinary skill in the art, In re Rose, 105 USPQ 237 (CCPA 1995), and discovery of the workable ranges involves only routine skill in the art, In re Aller, 105, USPQ 233.

32. Therefore, it would have been obvious for a person with ordinary skill in the art to be motivated using less dosage of therapeutic agent in combination of the oncolytic reovirus to treat ras-mediated neoplasm with much better anti-tumor effect since reovirus is particularly suitable for oncolyzing the ras-mediated neoplastic cell and combination of reovirus with a chemotherapeutic agent produces a synergistic effect. The claimed invention is prima facie obvious absence unexpected results.

33. Claims 1, 4, 8, 12, 17, 19, 20, 22, 26 are rejected under 35 U.S.C. 102(b) as being anticipated by William et al. (Cancer Immunol. Tmmunother. 1986, Vol. 23 (2), pp. 87-92) in view of Liu (Zhonghua Yi Xue Za Zhi 1993, Vol. 73, No. 9, pp. 552-664, 556) and Smith et al. (Exp. Opin. Invest. Drugs, 2000, Vol. 9, No. 2, pages 311-327).

34. William teach a method of treating neoplastic cells with a chemotherapeutic compound BCNU and reovirus in vitro and inhibit the tumor cell proliferation and growth (See entire document). Regarding to the limitations of the recitation of “sensitizing” or “preventing” a neoplastic cell to a chemotherapeutic agent, Office considered these recitation as preamble languages, which do not change the manipulating steps of the method comprising administration of reovirus and a chemotherapeutic agent into a population of neoplastic cells that result in a

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reduction of the neoplastic cells growth in vitro. William et al. do not teach that the reovirus is suitable for using with reovirus, and combination of reovirus and a chemotherapeutic agent can reduce the dosage of the chemotherapeutic agent. Moreover, applicants previously argue that leukemia cell line L1210 does not express oncogenic Ras.

35. Liu discloses that leukemia cell line L1201, especially the cis-platinum resistant cell line has enhanced oncogenes including C-myc, v-erb-B and N-ras expressions (See abstract).

36. Smith et al. teach that oncolytic reovirus treatment of cancer is particularly susceptible and effective for the ras-mutated cancer, and combined oncolytic reovirus and a chemotherapeutic agent treatment is more superior to any of the agent used alone. For reovirus, such synergistic therapeutic effect can produce a rate of 80% complete tumor remission (See pages 319, 1<sup>st</sup> paragraph of section 7 and 1<sup>st</sup> paragraph of section 9 on page 321).

37. Regarding to the precise number of less than 20% amount, applicants are reminded that the modification of working condition is generally recognized as being within the level of the ordinary skill in the art, In re Rose, 105 USPQ 237 (CCPA 1995), and discovery of the workable ranges involves only routine skill in the art, In re Aller, 105, USPQ 233.

38. Therefore, it would have been obvious for a person with ordinary skill in the art to be motivated using less dosage of therapeutic agent in combination of the oncolytic reovirus to treat ras-mediated neoplasm with much better anti-tumor effect since reovirus is particularly suitable for oncolyzing the ras-mediated neoplastic cell and combination of reovirus with a chemotherapeutic agent produces a synergistic effect. The claimed invention is prima facie obvious absence unexpected results.

39.

### ***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 7:00 am to 3:00 pm.

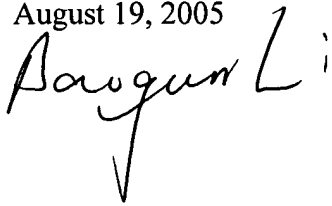
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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Baoqun Li MD

August 19, 2005

A handwritten signature in black ink that reads "Baoqun Li". The signature is written in a cursive style, with the first name "Baoqun" and the last name "Li" clearly distinguishable. There is a small vertical mark below the "i" in "Li".